CLAIMS

1. An anti-IFN-gamma polypeptide comprising at least one anti-IFN-gamma single domain antibody.

2. An anti-IFN-gamma polypeptide according to claim 1, wherein at least one anti-IFN-gamma single domain antibody, is a *Camelidae* VHH antibody.

3. An anti-IFN-gamma polypeptide according to claims 1 and 2 wherein at least one single domain antibody corresponds to a sequence represented by any of SEQ ID NOs: 1 to 35

4. An anti-IFN-gamma polypeptide according to any of claims 1 to 3 further comprising at least one single domain antibody directed against a serum protein.

5. An anti-IFN-gamma polypeptide according to claims 4 wherein a serum protein is any of serum albumin, serum immunoglobulins, thyroxine-binding protein, transferring, or fibrinogen.

6. An anti-IFN-gamma polypeptide according to claims 4 and 5 wherein an anti-serum protein single domain antibody correspond to a sequence represented by any of SEQ ID NOs: 36 to 39 and 62 to 74.

7. An anti-IFN-gamma polypeptide according to any of claims 4 to 6 corresponding to a sequence represented by any of SEQ ID NOs: 40 to 42.

8. An anti-IFN-gamma polypeptide according to any of claims 1 to 6 further comprising at least one single domain antibody selected from the group consisting of anti-TNF-alpha single domain antibody, anti-TNF-alpha receptor single domain antibody and anti-IFN-gamma receptor single domain antibody.

9. An anti-IFN-gamma polypeptide according to any of claims 1 to 7, wherein the number of single domain antibodies directed against IFN-gamma is at least two.

10. An anti-IFN-gamma polypeptide according to claim 9 corresponding to a sequence represented by any of SEQ ID NOs: 59 to 61.

11. An anti-IFN-gamma polypeptide according any of claims 1 to 10, wherein at least one single domain antibody is a humanized *Camelidae* VHHs.

12. A composition comprising an anti-IFN-gamma polypeptide according to any of claims 1 to 11 together with at least one single domain antibody from the group consisting of anti-TNF-alpha single domain antibody, anti-TNF-alpha receptor single domain antibody and anti-IFN-gamma receptor single domain antibody, for simultaneous, separate or sequential administration to a subject.

13. An anti-IFN-gamma polypeptide according to any of claims 7 to 11, or a composition according to claim 12 wherein at least one anti-TNF-alpha single domain antibody correspond to a sequence represented by any of SEQ ID NOs: 43 to 58.

14. An anti-IFN-gamma polypeptide according to any of claims 1 to 11, and 13, or a composition according to claims 12 and 13, wherein said single domain antibody is an homologous sequence, a functional portion, or a functional portion of an homologous sequence of the full length single domain antibody.

15. An anti-IFN-gamma polypeptide according to any of claims 1 to 11, 13 and 14, or a composition according to claims 12 to 14, wherein the anti-IFN-gamma polypeptide is an homologous sequence, a functional portion, or a functional portion of an homologous sequence of the full length anti-IFN-gamma polypeptide.

16. An anti-IFN-gamma polypeptide according to any of claim 1 to 11, and 13 to 15, or a composition according to claims 12 to 15 wherein said single domain antibodies are *Camelidae* VHHs.

17. A nucleic acid encoding an anti-IFN-gamma polypeptide according to any of claims 1 to 16.

18. A method of identifying an agent that modulates the binding of an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16, to IFN-gamma comprising the steps of:

(a) contacting an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 with a target that is IFN-gamma, in the presence and absence of a candidate modulator under conditions permitting binding between said polypeptide and target, and

(b) measuring the binding between the polypeptide and target of step (a), wherein a decrease in binding in the presence of said candidate modulator, relative to the binding in the absence of said candidate modulator identified said candidate modulator as an agent that modulates the binding of an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 and IFN-gamma.

19. A method of identifying an agent that modulates IFN-gamma-mediated disorders through the binding of an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 to IFN-gamma comprising:

(a) contacting an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 with a target that is IFN-gamma, in the presence and absence of a candidate modulator under conditions permitting binding between said polypeptide and target, and

(b) measuring the binding between the polypeptide and target of step (a), wherein a decrease in binding in the presence of said candidate modulator, relative to the binding in the absence of said candidate modulator identified, said candidate modulator as an agent that modulates IFN-gamma-mediated disorders.

20. A method of identifying an agent that modulates the binding of IFN-gamma to its receptor through the binding of an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 to IFN-gamma comprising:

(a) contacting an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 with a target that is IFN-gamma, in the presence and absence of a candidate modulator under conditions permitting binding between said polypeptide and target, and

(b) measuring the binding between the polypeptide and target of step (a), wherein a decrease in binding in the presence of said candidate modulator, relative to the binding in the absence of said candidate modulator identified said candidate modulator as an agent that modulates the binding of IFN-gamma to its receptor.

21. A kit for screening for agents that modulate IFN-gamma-mediated disorders comprising an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 and IFN-gamma.

22. An unknown agent that modulates the binding of an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 to IFN-gamma, identified according to the method of claim 18.

23. An unknown agent that modulates IFN-gamma-mediated disorders, identified according to the methods of claims 19 and 20.

24. An unknown agent according to claim 23 wherein said disorders are one or more of inflammation, rheumatoid arthritis, Crohn's disease, ulcerative colitis, inflammatory bowel syndrome and multiple sclerosis.

25. An anti-IFN-gamma polypeptide according to any of claims 1 to 11, and 13 to 16, or a nucleic acid according to claim 17, or a composition according to any of claims 12 to 16, or an agent according to any of claims 22 to 24 for treating and/or preventing and/or alleviating disorders relating to inflammatory processes.

26. Use of an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 or a nucleic acid according to claim 17, or a composition according to any of claims 12 to 16, or an agent according to any of claims 20 to 21 for the preparation of a medicament for treating and/or preventing and/or alleviating disorders relating to inflammatory reactions.

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27. An anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 or a composition according to any of claims 12 to 16, for treating and/or preventing and/or alleviating disorders requiring the delivery of a IFN-gamma modulating polypeptide that is able pass through the gastric environment without being inactivated.

28. Use of an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 or a composition according to any of claims 12 to 16, for the preparation of a medicament for treating, preventing and/or alleviating the symptoms of disorders requiring the delivery of a IFN-gamma modulating polypeptide that is able pass through the gastric environment without being inactivated.

29. An anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 or a composition according to any of claims 12 to 16, for treating and/or preventing and/or alleviating disorders requiring the delivery of a IFN-gamma modulator to the vaginal and/or rectal tract.

30. Use of an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 or a composition according to any of claims 12 to 16, for the preparation of a medicament for treating, preventing and/or alleviating the symptoms of disorders requiring the delivery of a IFN-gamma modulator to the vaginal and/or rectal tract.

31. An anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 or a composition according to any of claims 12 to 16, for treating and/or preventing and/or alleviating disorders requiring the delivery of a therapeutic compound to the upper respiratory tract and lung.

32. Use of an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 or a composition according to any of claims 12 to 16, for the preparation of a medicament for treating, preventing and/or alleviating the symptoms of disorders requiring the delivery of a therapeutic compound to the upper respiratory tract and lung.

33. An anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 or a composition according to any of claims 12 to 16, for treating and/or preventing and/or alleviating disorders requiring the delivery of a IFN-gamma modulator, wherein said disorder increases the permeability of the intestinal mucosa.

34. Use of an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 or a composition according to any of claims 12 to 16, for the preparation of a medicament for treating, preventing and/or alleviating the symptoms of disorders requiring the delivery of a IFN-gamma modulator, wherein said disorder increases the permeability of the intestinal mucosa.

35. An anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 or a composition according to any of claims 12 to 16, for treating and/or preventing and/or alleviating disorders requiring delivery of a IFN-gamma modulator that is able pass through the tissues beneath the tongue.

36. Use of an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 or a composition according to any of claims 12 to 16, for the preparation of a medicament for treating, preventing and/or alleviating the symptoms of disorders requiring delivery of a IFN-gamma modulator that is able pass through the tissues beneath the tongue.

37. An anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 or a composition according to any of claims 12 to 16, for treating and/or preventing and/or alleviating disorders requiring delivery of a IFN-gamma modulator that is able pass through the skin.

38. Use of an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 or a composition according to any of claims 12 to 16, for the preparation of a medicament for treating, preventing and/or alleviating the symptoms of disorders requiring delivery of a IFN-gamma modulator that is able pass through the skin.

39. A method according to claim 19, a kit according to claim 21, a nucleic acid or agent according to claim 25, use of a nucleic acid or agent according to claim 26, a composition according to any of claims 25, 27, 29, 31, 33, 35, 37 and 39, use of a composition according to any of claims 26, 28, 30, 32, 34, 36, and 38, an anti-IFN-gamma polypeptide of any of claims 25, 27, 29, 31, 33, 35, 37 and 39, use of an anti-IFN-gamma polypeptide according to any of claims 26, 28, 30, 32, 34, 36, and 38 wherein said disorders are any of inflammation, rheumatoid arthritis, Crohn's disease, ulcerative colitis, inflammatory bowel syndrome, multiple sclerosis, Addison's disease, Autoimmune hepatitis, Autoimmune parotitis, Diabetes Type I, Epididymitis, Glomerulonephritis, Graves' disease, Guillain-Barre syndrome, Hashimoto's disease, Hemolytic anemia, Systemic lupus erythematosus, Male infertility, Multiple sclerosis, Myasthenia Gravis, Pemphigus, Psoriasis, Rheumatic fever, Rheumatoid arthritis, Sarcoidosis, Scleroderma, Sjogren's syndrome, Spondyloarthropathies, Thyroiditis, and Vasculitis.

40. A composition comprising a nucleic acid or agent according to claim 25, an anti-IFN-gamma polypeptide of any of claims 1 to 11 and 13 to 16, or a composition according to any of claims 12 to 16, and a suitable pharmaceutical vehicle.

41. A method of diagnosing a disorder characterised by the dysfunction of IFN-gamma comprising:

(a) contacting a sample with an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16,

(b) detecting binding of said polypeptide to said sample, and

(c) comparing the binding detected in step (b) with a standard, wherein a difference in binding relative to said sample is diagnostic of a disorder characterised by dysfunction of IFN-gamma.

42. A kit for screening for a disorder cited in claim 39, using a method according to claim 38.

43. A kit for screening for a disorder cited in claim 39 comprising an isolated anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16.

44. Use of an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 for the purification of said IFN-gamma.

45. Use of an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 for inhibiting the interaction between IFN-gamma and one or more IFN-gamma receptors.

46. A method for producing an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 comprising the steps of:

(a) obtaining double stranded DNA encoding a *Camelidae* VHH directed to IFN-gamma,

(b) cloning and expressing the DNA selected in step (b).

47. A method of producing an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16 comprising:

(a) culturing host cells comprising nucleic acid capable of encoding an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16, under conditions allowing the expression of the polypeptide, and,

(b) recovering the produced polypeptide from the culture.

48. A method according to claim 47, wherein said host cells are bacterial or yeast.

49. A kit for screening for any of inflammation, rheumatoid arthritis, Crohn's disease, ulcerative colitis, inflammatory bowel syndrome or multiple sclerosis comprising an anti-IFN-gamma polypeptide of any of claims 1 to 11, and 13 to 16.